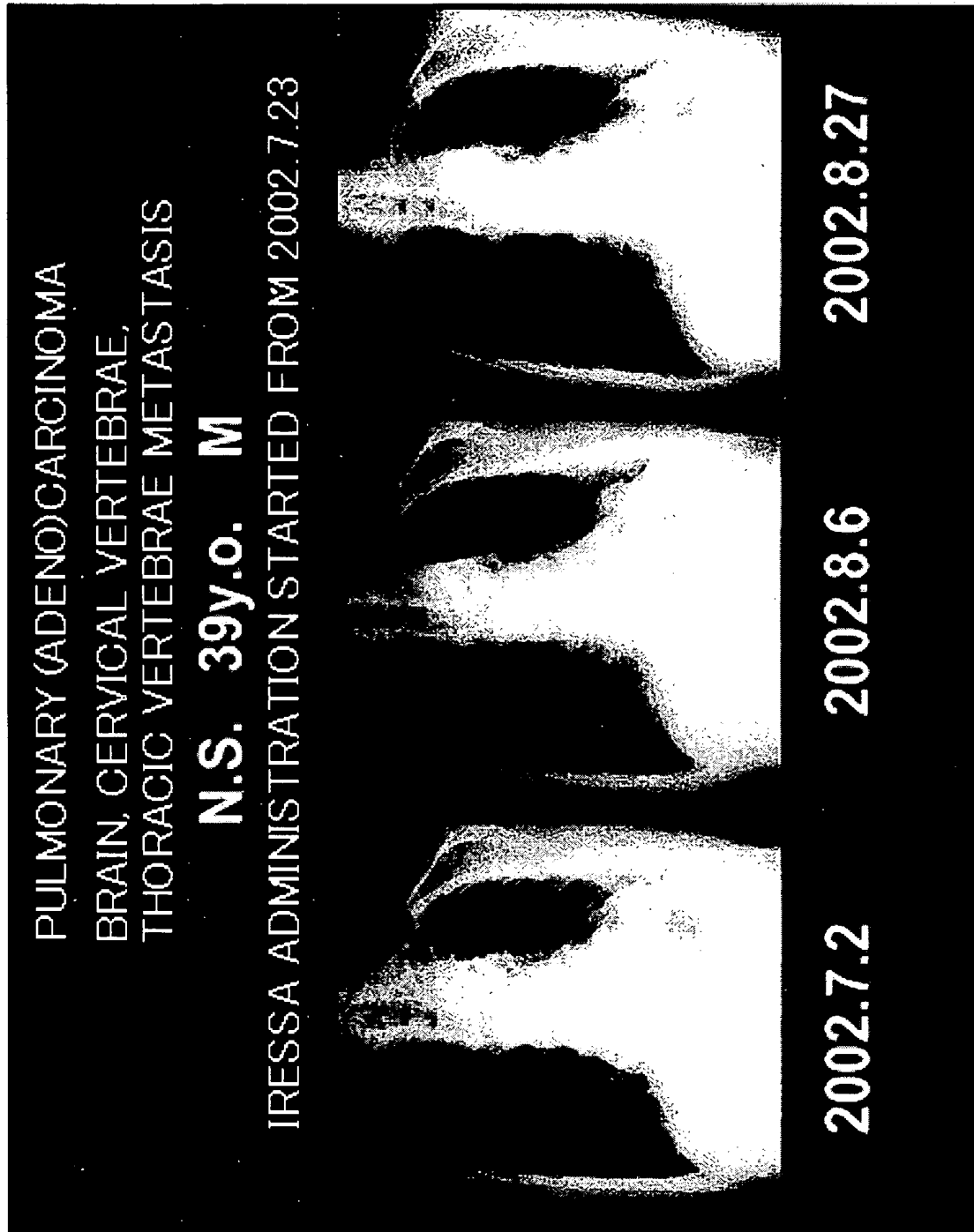


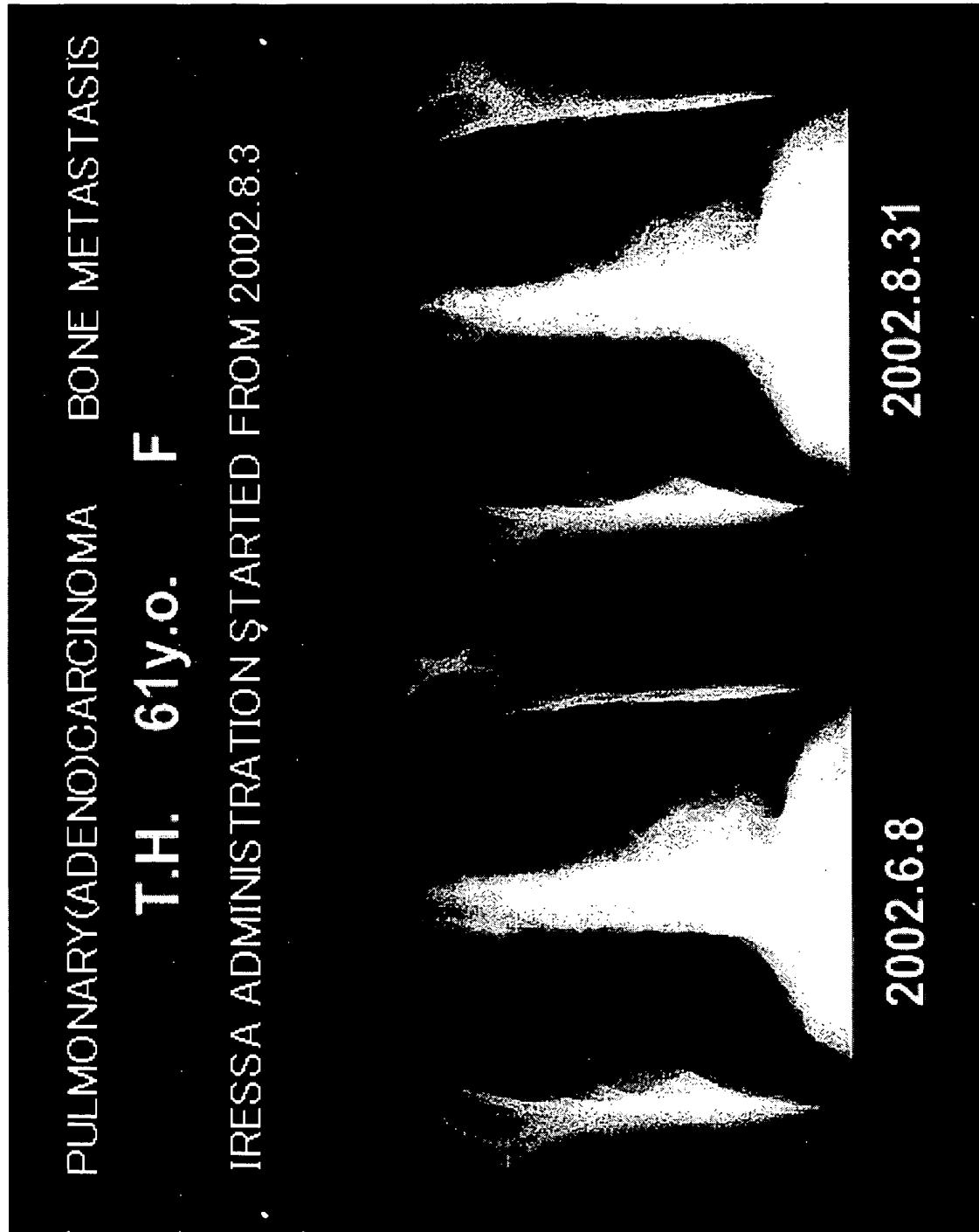
DRAWINGS

Figure 1



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Figure 2



ESSENTIAL SIGNALS FOR OSTEOCLAST DIFFERENTIATION

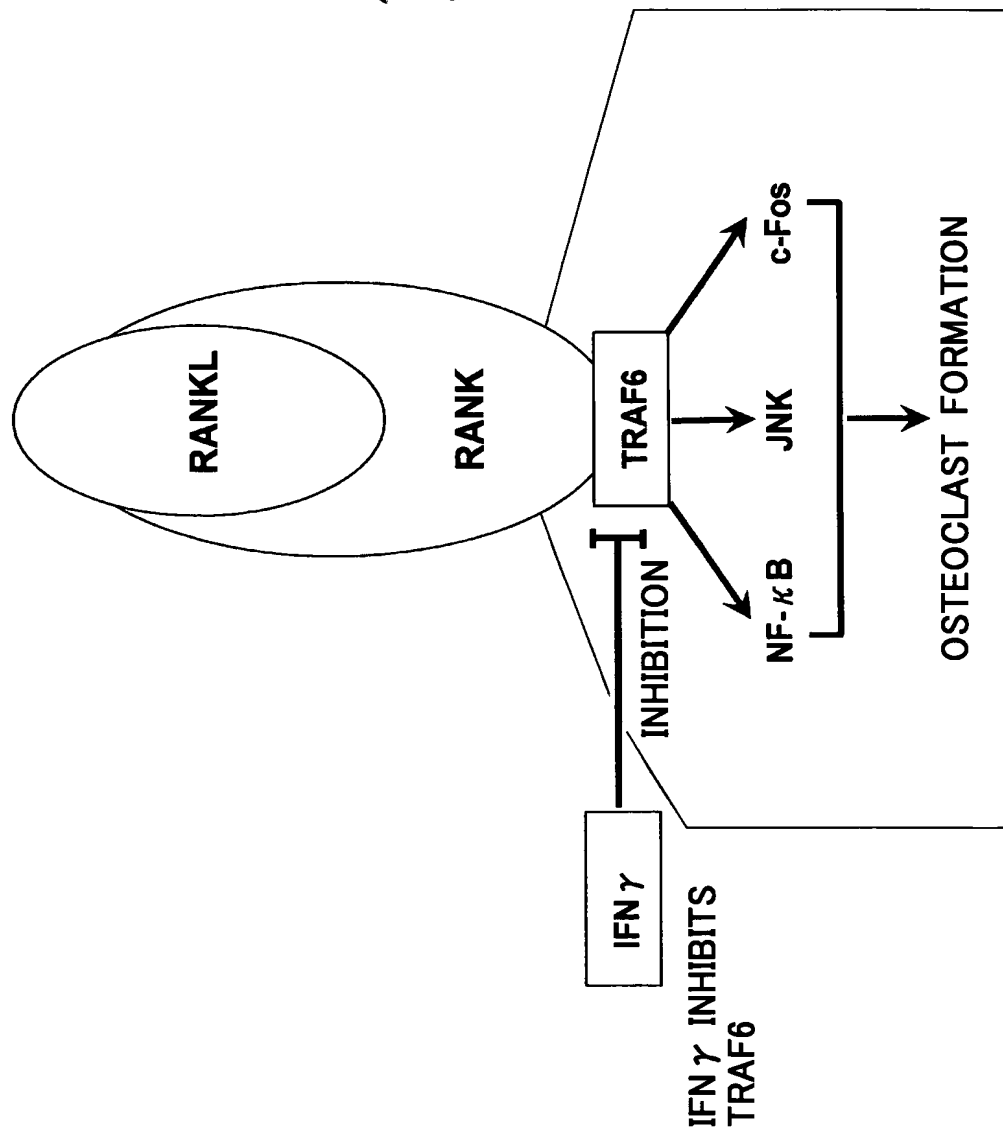


Figure 3

Figure 4

**EFFECTIVE CASES FOR PULMONARY ADENOCARCINOMA
(COMBINED THERAPY OF IRESSA AND NITC)**

| | | AGE | GEN- DER | METASTATIC FOCUS | RATING |
|----|------|-----|-------------|--|--------|
| 1 | T.H. | 61 | F | PLEURAPOPHYSIS | PR |
| 2 | N.S. | 39 | M | BRAIN, CERVICAL VERTEB- RAE, THORACIC VERTEBRAE | PR |
| 3 | H.T. | 78 | M | | PR~CR |
| 4 | F.T. | 66 | F | | PR |
| 5 | M.F. | 51 | F | | PR |
| 6 | C.I. | 59 | M | BOTH LUNGS. BONE (MULTIPLE) | PR |
| 7 | S.Y. | 69 | M | | PR |
| 8 | K.F. | 71 | F | BONE (MULTIPLE) | PR |
| 9 | K.M. | 74 | F | | PR |
| 10 | T.S. | 66 | F | | PR |
| 11 | O.K. | 69 | F | | PR |
| 12 | U.S. | 79 | F | INTRAPULMONARY | PR |
| 13 | I.Y. | 71 | M | BONE (MULTIPLE) | NC~PR |
| 14 | I.Y. | 73 | M | | NC~PR |
| 15 | O.K. | 57 | F | | NC |

RATE OF EFFICACY FOR PULMONARY

ADENOCARCINOMA : PR 12/15(80.0%)
: NC 3/15(20.0%)

Figure 5

EFFECTIVE CASES FOR CANCER OF THE LARGE INTESTINE
(COMBINED THERAPY OF IRESSA AND NITC)

COLON CANCER

| | AGE | GEN- DER | SITE | METASTATIC FOCUS | RAT- ING |
|---|---------|-------------|------|------------------------------|-------------|
| 1 | K.Y. 57 | F | C | | PR |
| 2 | S.I. 63 | F | S | CERVICAL LYMPH NODE | PR |
| 3 | M.K. 53 | M | A | CERVICAL LYMPH NODE, LUNG | PR |
| 4 | H.M. 51 | M | D | LIVER | PR |
| 5 | H.S. 64 | F | S | LIVER, BONE | PR |
| 6 | S.N. 67 | F | T | LUNG | NC |
| 7 | O.T. 63 | M | S+C | LUNG, LIVER | PD |

CANCER OF THE RECTUM

| | AGE | GEN- DER | METASTA- TIC FOCUS | RAT- ING |
|---|---------|-------------|-----------------------|-------------|
| 1 | Y.Y. 57 | M | LIVER | PR |
| 2 | O.T. 64 | M | (RECTUM+A) | PR |
| 3 | K.H. 60 | M | | PR |
| 4 | K.M. 64 | F | LUNG, LIVER | PR |

RATE OF EFFICACY FOR CANCER
OF THE COLON

: PR 5/7(71.4%)
: NC 1/7(14.3%)
: PD 1/7(14.3%)

RATE OF EFFICACY FOR CANCER
OF THE RECTUM

: PR 4/4(100%)

RATE OF EFFICACY FOR CANCER OF
THE LARGE INTESTINE

: PR 9/11(81.8%)
: NC 1/11(9.1%)
: PD 1/11(9.1%)

Figure 6

**EFFECTIVE CASES OF COMBINED
TREATMENT WITH IRESSA AND NITG**

| | PR | NC | PD | TOTAL n NUMBER |
|----------------------------------|------------|------------|------------|-------------------|
| PULMONARY (ADE- NO) CARCINOMA | 12 (80.0%) | 3 (20.0%) | 0 (0%) | 15 |
| CANCER OF THE LARGE INTESTINE | 9 (81.8%) | 1 (9.1%) | 1 (9.1%) | 11 |
| COLON CANCER | 5 (71.4%) | 1 (14.3%) | 1 (14.3%) | 7 |
| CANCER OF THE RECTUM | 4 (100%) | | | 4 |
| ANAL CANCER | 1 (50%) | | 1 (50%) | 2 |
| RENAL CANCER | 2 (100%) | | | 2 |
| LINGUAL CANCER | 1 (100%) | | | 1 |
| BREAST CANCER | 1 (16.7%) | 1 (16.7%) | 4 (66.7%) | 6 |
| GASTRIC CANCER | 1 (33.3%) | | 2 (66.7%) | 3 |
| PROSTATIC CANCER | | 2 (100%) | | 2 |
| ESOPHAGEAL CANCER | | 2 (66.7%) | 1 (33.3%) | 3 |
| PANCREATIC CANCER | | 1 (100%) | | 1 |
| PHARYNGEAL CANCER | | 1 (100%) | | 1 |
| PAROTID CANCER | | 1 (100%) | | 1 |
| BLADDER CANCER | | | 2 (100%) | 2 |
| CERVICAL CANCER | | | 1 (100%) | 1 |
| OVARIAN CANCER | 2 (50.0%) | 1 (25.0%) | 1 (25.0%) | 4 |
| TOTAL | 29 (52.7%) | 13 (23.6%) | 13 (23.6%) | 55 |

Figure 7

DEGREE OF CONTRIBUTION FOR EFFICACY OF EACH MARKER
(PULMONARY ADENOCARCINOMA)

n=73 (27 SUBJECTS ADMINISTERED WITH
IRESSA, 46 SUBJECTS WITHOUT IRESSA
ADMINISTRATION)
p=0.700

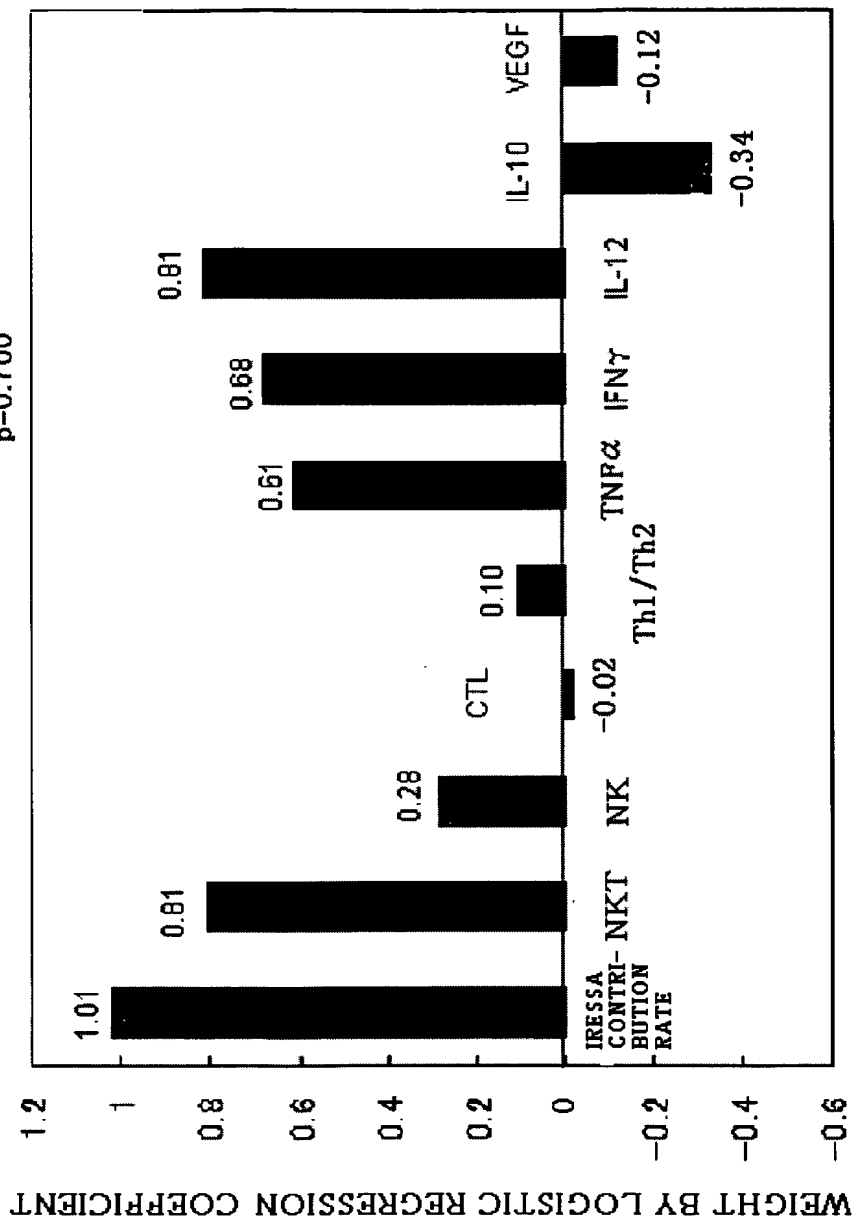
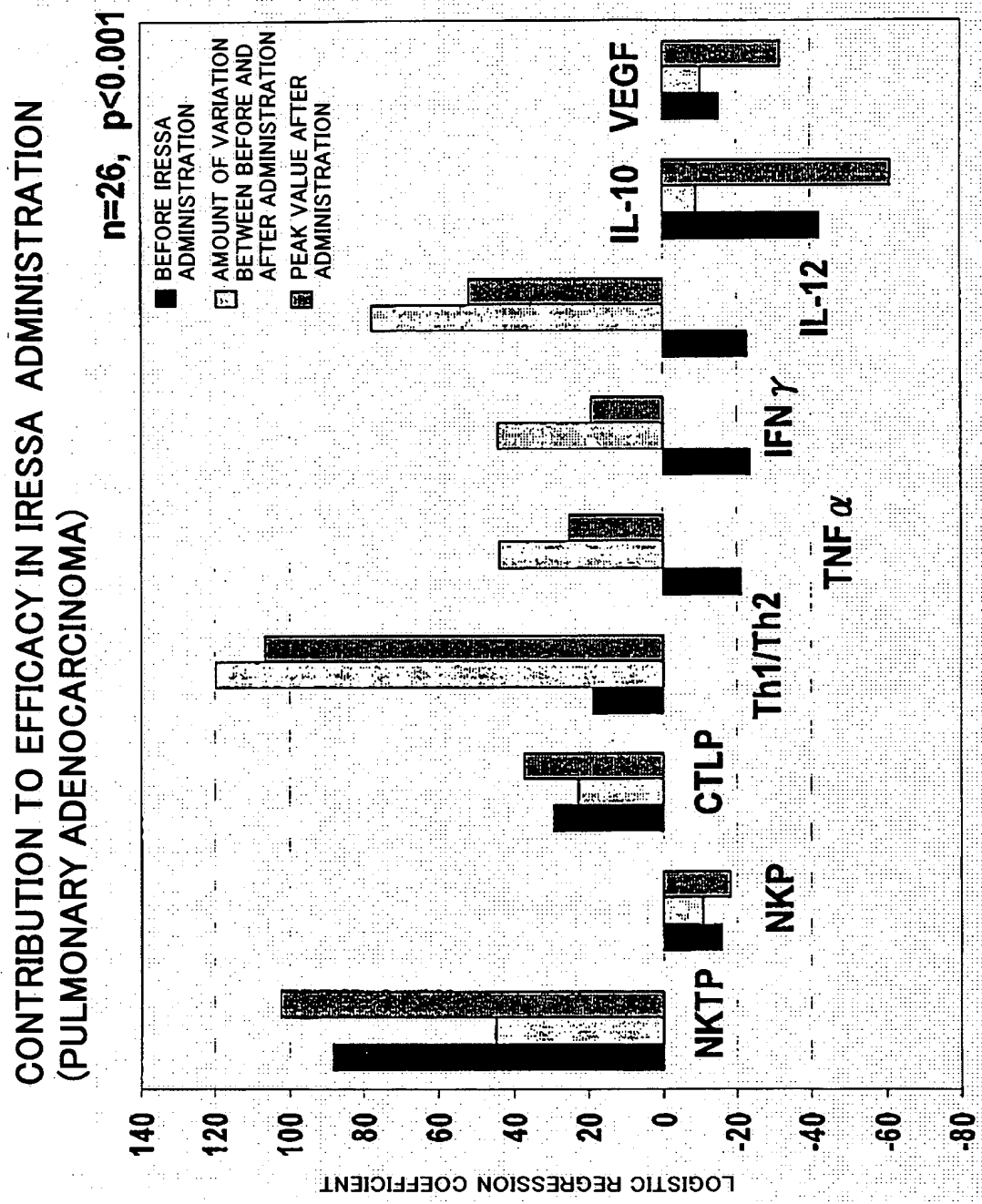


Figure 8



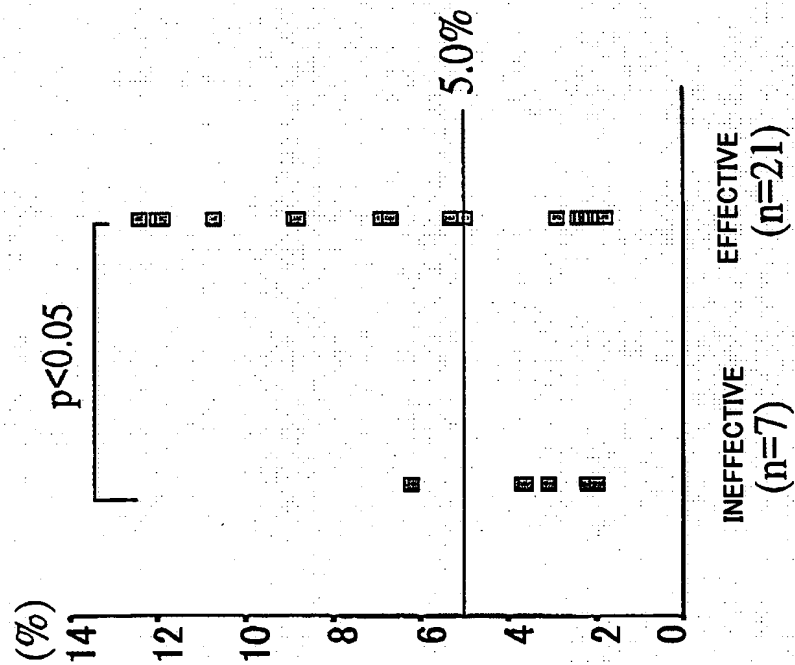
9/15

Figure 9

COMPARISON OF EFFECTIVE CASES (B GROUP) AND
INEFFECTIVE CASES (A GROUP) PRIOR TO IRESSA ADMINISTRATION

| NKT PERFORIN ACTIVITY (%) BEFORE IRESSA ADMINISTRATION | EFFECTIVE CASES | INEFFECTIVE CASES | TOTAL |
|--|--------------------|----------------------|-------|
| 5.0 OR MORE | 13 | 1 | 14 |
| LESS THAN 5.0 | 8 | 6 | 14 |
| TOTAL | 21 | 7 | 28 |

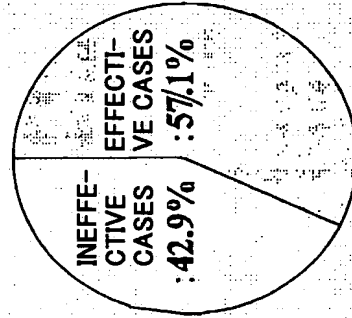
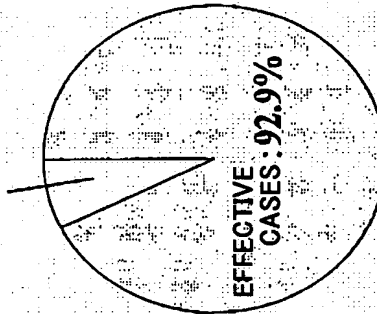
(p<0.05)



NKTP \geq 5.0

NKTP < 5.0

INEFFECTIVE CASES : 7.1%



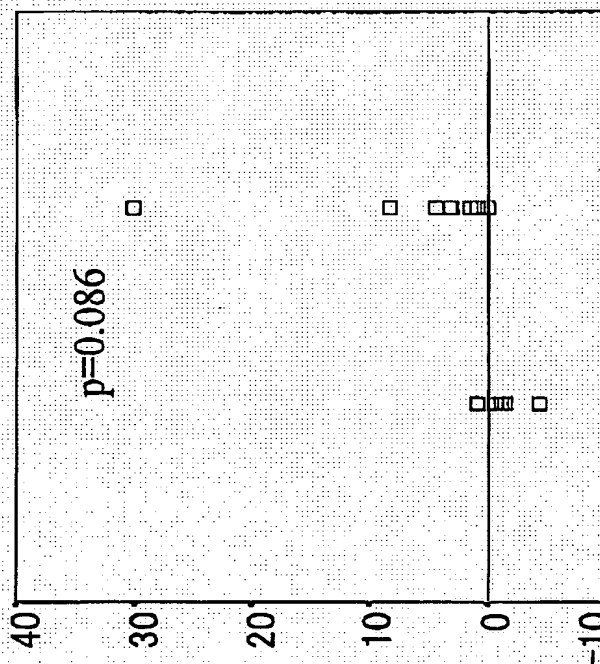
10/15

Figure 10

COMPARISON OF EFFECTIVE CASES (B GROUP) AND INEFFECTIVE CASES (A GROUP) FOR NKTP < 5.0

| VARIATION IN RATIO OF Th1/Th2 BEFORE AND AFTER IRESSA ADMINISTRATION | EFFECTIVE CASES | INEFFECTIVE CASES | TOTAL |
|--|-----------------|-------------------|-------|
| INCREASE | 8 | 1 | 9 |
| DECREASE | 0 | 5 | 5 |
| TOTAL | 8 | 6 | 14 |

(p<0.01)



Th1/Th2 INCREASED AFTER IRESSA ADMINISTRATION

Th1/Th2 DECREASED AFTER IRESSA ADMINISTRATION

INEFFECTIVE CASES: 11.1%

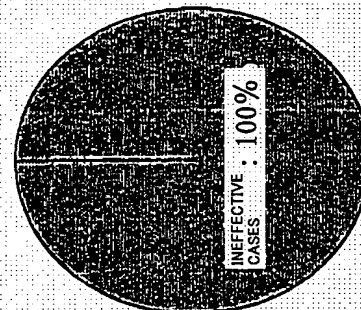
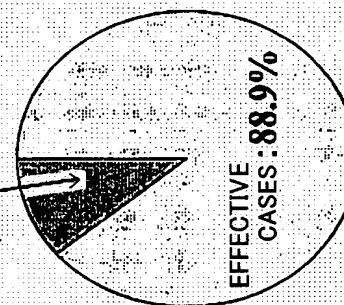


Figure 11

EFFECTIVE AND INEFFECTIVE GROUPS
ACCORDING TO 2 THRESHOLD VALUES

| | EFFECTIVE | INEFFECTIVE |
|--------------------------------------|-----------|-------------|
| NKTP \geq 5.0 OR Th1/Th2 INCREASED | 21 | 2 |
| NKTP < 5.0 AND Th1/Th2 DECREASED | 0 | 5 |
| TOTAL | 21 | 7 |

TEST BY CHI-SQUARE TEST
 $p < 0.001$

Figure 12

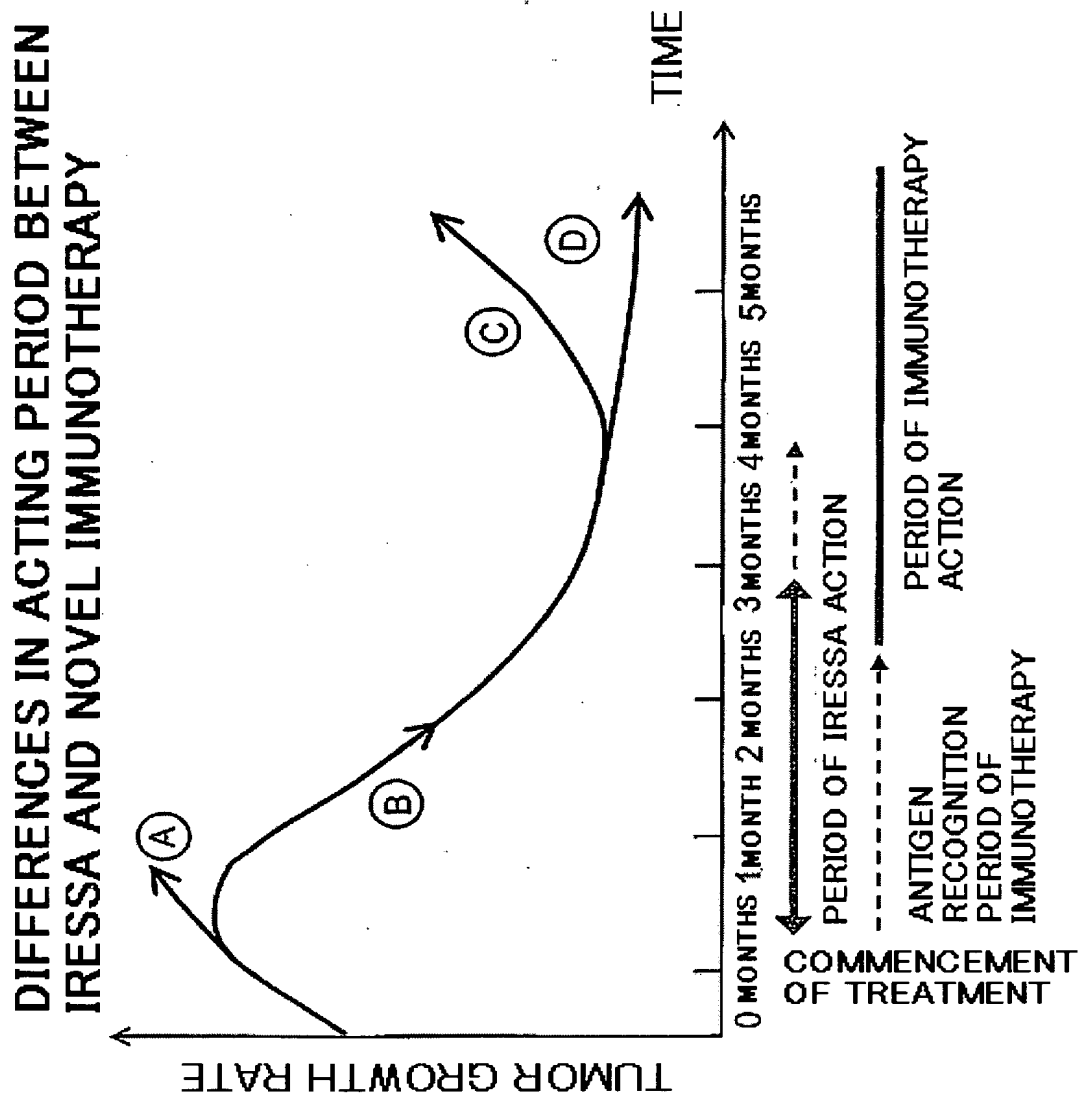
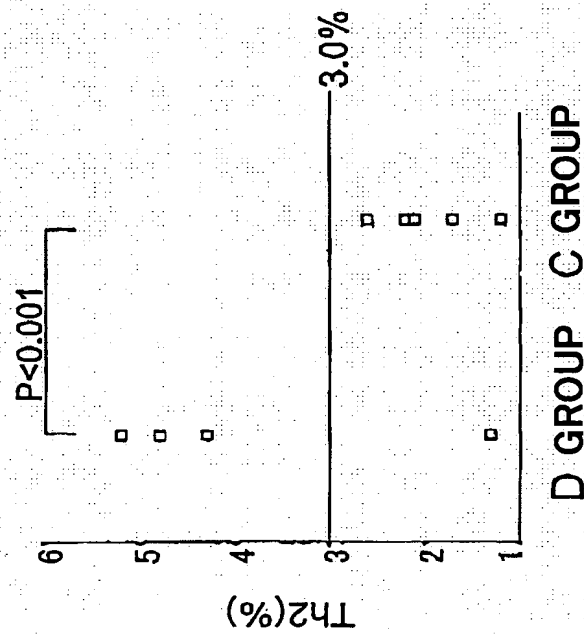


Figure 13

COMPARISON OF C GROUP AND D GROUP
PRIOR TO IRESSA



| TH2(%) BEFORE IRESSA ADMINISTRATION | C GROUP | D GROUP | TOTAL |
|---|------------|------------|-------|
| 3.0 OR MORE | 0 | 5 | 5 |
| LESS THAN 3.0 | 5 | 1 | 6 |
| TOTAL | 5 | 6 | 11 |

($p < 0.05$)

Figure 14

CYTOKINE DIFFERENCES IN C GROUP AND D GROUP

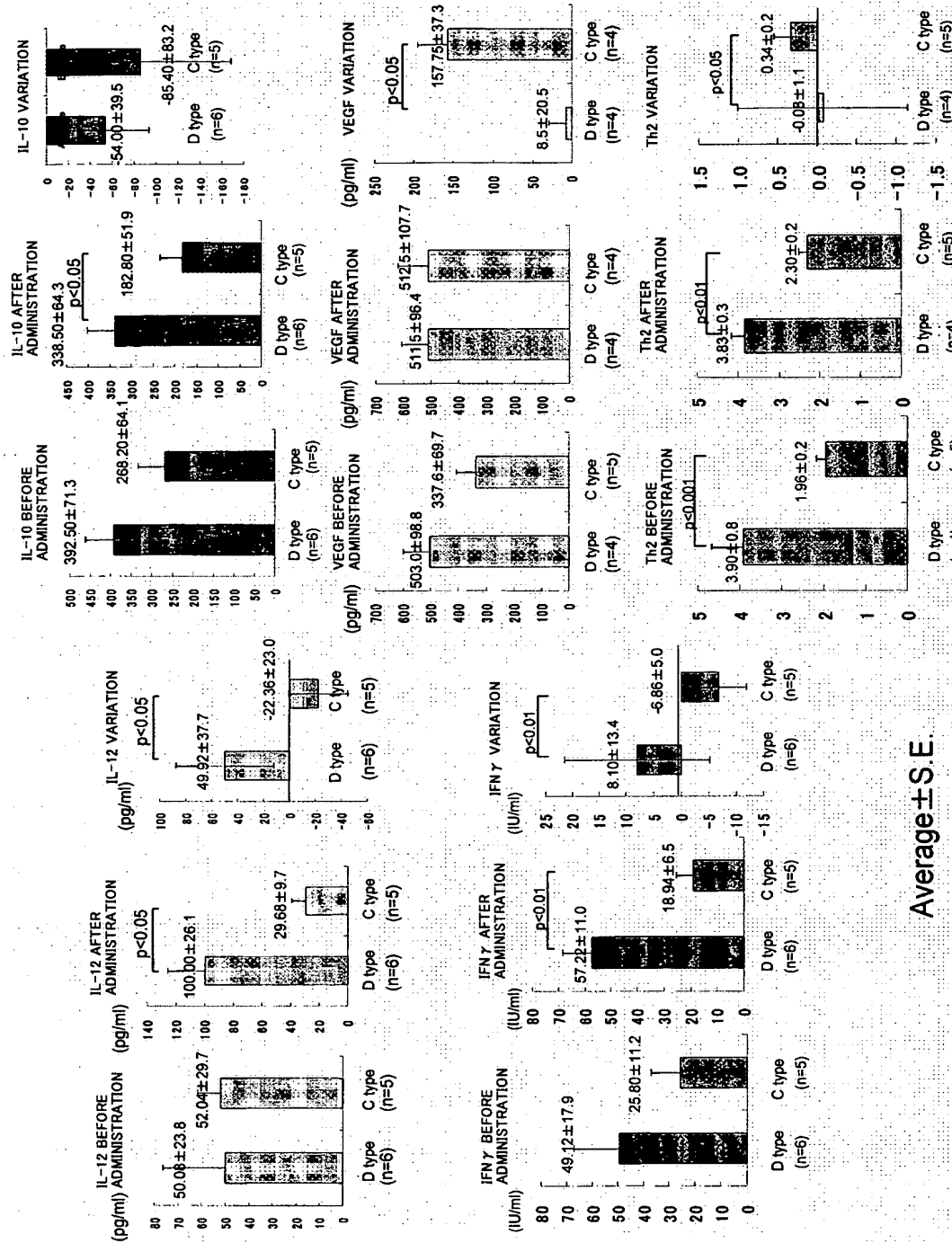
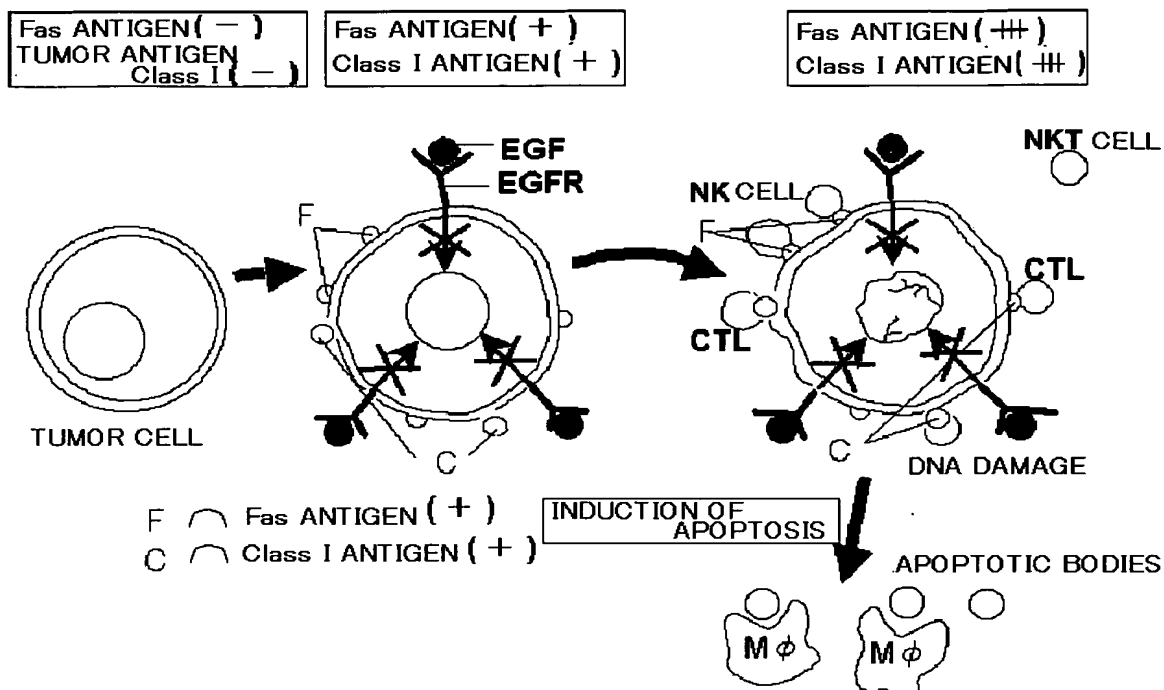


Figure 15

MECHANISM OF SYNERGISTIC ACTION OF IRESSA AND NITC (HYPOTHESIS)



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